# Therapeutic Management of Carious Injuries in Chronic Graft-Versus-Host Disease Patients: Case Report

doi: https://doi.org/10.32635/2176-9745.RBC.2020v66n2.932

*Manejo Terapêutico das Lesões Cariosas em Pacientes com a Doença do Enxerto contra o Hospedeiro Crônica: Relato de Caso*

Manejo Terapéutico de Lesiones Cariosas en Pacientes con Enfermedad del Huésped Injerto contra Huésped Crónica: Reporte de un Caso

**Ana Carolina da Silva Souto[1]; Gabriela de Assis Ramos[2]; Andreia Cristina Melo[3]; Daniel Cohen Goldemberg[4]; Héliton Spíndola Antunes[5]**

***Abstract***

**Introduction:** Chronic graft-versus-host disease (cGVHD) is the main cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (HSCT-alo). **Case Report:** Dental follow-up of a 59-year-old male patient, with initial diagnosis of acute myeloid leukemia, who underwent HSCT-alo in May 2017. At D+ 224, the patient developed a condition of GVHD affecting the skin, oral cavity and gastrointestinal tract, but with still healthy teeth. On D+ 392, the patient complained of dry mouth, oral lesions were observed, and sialometry was 0.024mL/min, with evolution of carious lesions on teeth 17, 15, 22, 25, 27, 38, 45 and 46. At D+ 560, the patient still had oral GVHD and the progression of caries was observed in numerous teeth. **Treatment and Results:** The therapeutic management adopted consisted of the use of silver diamine fluoride due to its cariostatic property with reduced tooth pain and later dental restorations were performed. In addition, the patient received guidance about diet, maintenance of oral hygiene and use of oral lubricant to ease xerostomia. **Conclusion:** It was observed in this clinical case that silver diamine fluoride was effective in controlling the evolution of caries and reducing tooth pain in adult patients. It is evident the importance of training dentists on the knowledge about the use of cariostatic resources in patients with changes in the quality and quantity of saliva, such as patients with oral GVHD.

**Key words:** Cariostatic Agents; Graft vs Host Disease; Oral Manifestations; Case Reports.

Resumo

**Introdução:** A doença do enxerto contra o hospedeiro crônica (DECHc) é a principal causa de morbimortalidade após o transplante alogênico de células-tronco hematopoiéticas (TCTH-alo). **Relato do Caso:** Acompanhamento odontológico de paciente do sexo masculino, 59 anos, com diagnóstico inicial de leucemia mieloide aguda, submetido ao TCTH-alo em maio de 2017. No D+ 224, o paciente evoluiu para um quadro de DECHc acometendo a pele, a cavidade oral e o trato gastrointestinal, porém com dentes ainda hígidos. No D+ 392, o paciente queixou-se de boca seca, e foram observadas lesões orais, sialometria de 0,024 mL/min e evolução de lesões cariosas nos dentes 17, 15, 22, 25, 27, 38, 45 e 46. No D+ 560, o paciente ainda estava com DECHc oral e houve progressão das cáries em inúmeros dentes. **Tratamento e Resultados:** O manejo terapêutico adotado consistiu na utilização de diamino fluoreto de prata pela propriedade cariostática com redução da odontalgia e, posteriormente, foram realizadas as restaurações dentárias. Além disso, o paciente foi orientado em relação à dieta, à manutenção da higiene oral e ao uso de lubrificante oral na tentativa de amenizar a xerostomia. **Conclusão:** Observou-se, neste caso clínico, que o diamino fluoreto de prata foi eficaz no controle da evolução da cárie e redução da odontalgia no paciente adulto. É evidente a importância da capacitação dos cirurgiões-dentistas no que diz respeito ao conhecimento sobre a utilização de cariostáticos em pacientes com alterações na qualidade e quantidade de saliva como os pacientes com DECHc oral.

**Palavras-chave:** Cariostáticos; Doença Enxerto-Hospedeiro; Manifestações Bucais; Relatos de Casos.

Resumen

**Introducción:** La enfermedad crónica del huésped versus el injerto (cGVHD) es la principal causa de morbilidad y mortalidad después del trasplante alogénico de células madre hematopoyéticas (HSCT-alo). **Relato del Caso:** Seguimiento dental de un paciente masculino de 59 años, con diagnóstico inicial de leucemia mieloide aguda, que se sometió a un HSCT-alo en mayo de 2017. En D+ 224, el paciente desarrolló una condición de EICH que afecta la piel, la cavidad oral y el tracto gastrointestinal, pero con dientes aún sanos. En D+ 392, el paciente se quejó de sequedad en la boca y se observaron lesiones orales y con sialometría de 0,024 ml/min. También presentó evolución de lesiones cariosas en los dientes 17, 15, 22, 25, 27, 38, 45 y 46. En D+ 560, el paciente todavía tenía EICH oral y se observó la progresión de la caries en numerosos dientes. **Tratamiento y Resultados:** El tratamiento terapéutico adoptado consistió en el uso de diamino fluoruro de plata debido a su propiedad cariostática con reducción del dolor dental y posteriormente se realizaron restauraciones dentales. Además, el paciente recibió instrucciones sobre la dieta, el mantenimiento de la higiene bucal y el uso de lubricante oral en un intento por aliviar la xerostomía. **Conclusión:** Se observó en este caso clínico que el diamino fluoruro de plata fue efectivo para controlar la evolución de la caries y reducir el dolor dental en pacientes adultos. Es evidente la importancia de capacitar a los dentistas con respecto al conocimiento sobre el uso de recursos cariostáticos en pacientes con cambios en la calidad y cantidad de saliva, como los pacientes con EICH oral.

**Palabras clave:** Cariostáticos; Enfermedad Injerto contra Huésped; Manifestaciones Bucales; Informes de Casos.

[1]Undergraduate of Scientific Initiation of the Coordination of Clinical Research of the National Cancer Institute José Alencar Gomes da Silva (INCA). Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-2438-5860
[2]Coordination of Clinical Research of INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0001-9689-8692
[3]Coordination of Clinical Research of INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-1201-4333
[4]Coordination of Clinical Research of INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-0089-1910
[5]Coordination of Clinical Research of INCA. Rio de Janeiro (RJ), Brazil. Orcid iD: https://orcid.org/0000-0002-1076-8019
Address for Correspondence: Ana Carolina da Silva Souto. Divisão de Pesquisa Clínica do INCA. Rua André Cavalcante, 37, 2º andar – Centro. Rio de Janeiro (RJ), Brazil. CEP 20231-050. E-mail: soutocarolll@gmail.com

## INTRODUCTION

The chronic graft versus host disease (cGVHD) is considered one of the main causes of morbimortality after allogeneic hematopoietic stem cells transplantation (HSCT-alo), affecting 30% to 70% of the patients[1]. The clinical manifestations are most common during the first year post-HSCT but can occur years after the transplantation. Its symptomatology may be restricted to a single organ or can be disseminated, influencing directly the quality of life of the patient[2].

One of the most frequent locations of cGVHD is the oral cavity[3]. The oral clinical characteristics commonly found involve lichenoid lesions, manifesting erythematous surfaces with hyperkeratotic furrows, generally encountered in the jugal mucosa and/or tongue but can also involve other intraoral surfaces and the labial region[4]. Despite not being considered diagnostic lesions of oral cGVHD, atrophic areas, ulcers covered with pseudo membrane and microstomia associated to dermal sclerosis of perioral areas[5] are found.

The cGVHD, for being a syndrome with clinical manifestations similar to autoimmune diseases, is able to interfere in the functioning of the salivary glands, resulting in hyposalivation. It reduces the protective role of oral tissues by the saliva making patients more susceptible to carious lesions[6]. Carious lesions are seen mainly in cervical and proximal regions[7]. Palliative care to minimize hyposalivation and avoid caries imply in constant intake of water, sugar-free gums or candies, buccal gel with the objective of humidifying the oral mucosa, application of sodium fluoride and effective dental brushing[8]. It is of the utmost importance that the patient with cGVHD is followed up by a multi-disciplinary team including surgeon-dentist to maintain the integrity of the buccal tissues and effective oral hygiene to prevent future complications.

In the cases where there is caries diagnosis, silver diamine fluoride can be applied among other therapeutic options[9]. It is a simple, low cost, minimally invasive medicament that can also be used in therapeutic management in situations of hypersensitiveness[10]. Studies indicate that it is able to arrest caries successfully and in situations where caries is deep, partial removal of caries is advised for improved remineralization, more preservation of the dental structure, restauration of the functions and improvement of the vitality of the pulp[11].

In the clinical case addressed below, caries management and restorative treatment of a patient with diagnosis of cGVHD are described.

## CASE REPORT

Male, 59 years old, initial diagnosis of acute myeloid leukemia, submitted to related HSCT-alo on May 2017. In the first post-HSCT odontology evaluation on May 25, 2017 (D+ 91) there was no diagnosis of systemic cGVHD or clinical sign of oral cavity lesion and the dental elements were healthy. On October 10, 2017 (D+ 224), the patient evolved to a condition of cGVHD affecting the skin, oral cavity and gastrointestinal tract but with teeth still healthy (Figure 1). On March 22, 2018 (D+ 392), the patient complained of dry mouth, sialometry of 0.024 mL/min was measured and white oral lesions were observed, affecting: right jugal mucosa extending to retromolar trigone until labial commissure; left jugal mucosa extending to retromolar trigone up to labial commissure; left lower labial mucosa and in the region of the hard palate extending up to the left and right gum borders. Evolution to carious lesions in dental elements 17, 15, 22, 25, 27, 38, 45 and 46 (Figure 2 and 3) was observed. On September 6, 2018 (D+560) the patient was still in oral cGVHD and it was observed the progression of the caries in innumerous dental elements.

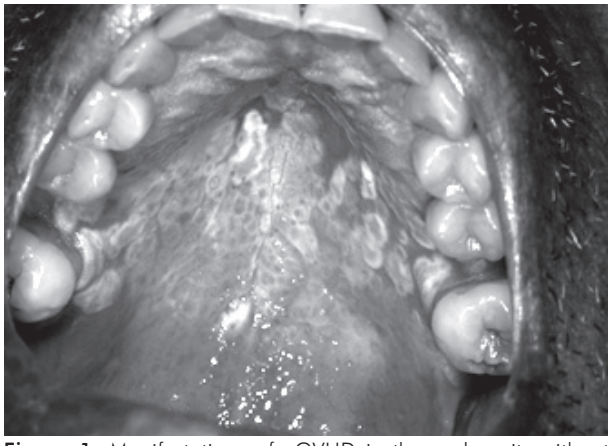
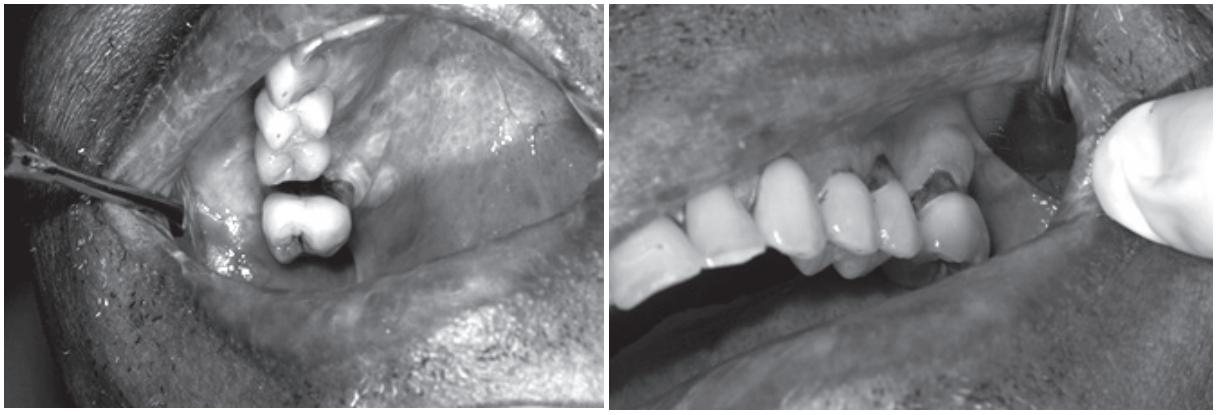


**Figure 1.** Manifestations of cGVHD in the oral cavity without compromise of the teeth in D+ 224

## TREATMENT AND RESULTS

The therapeutic management adopted consisted in the application of silver fluoride diamine with cariostatic goal in the cervical region of the teeth 17, 15, 25, 27, 28, 38, 37, 36, 32, 31, 41, 42, 46, 47 in September 2018. In addition, the patient received dietary, buccal hygiene guidance and use of oral lubricant (Bioxtra Oral Gel®) in the oral mucosa, six times a day, attempting to minimize xerostomia. In November 2018, after clinical and radiographic examination, arrest of the carious activity and odontalgia were observed. Further, caries were removed and dental restorations with photopolymerizable composite resin were made.



**Figures 2 and 3.** Manifestations of cGVHD in the oral cavity and rampant carious lesions. D+ 560

## DISCUSSION

The HSCT-alo is a potentially curative therapeutic modality, essential for the treatment of innumerous diseases, including hematopoietic neoplasms[12]. However, these patients can evolve to a succession of post-HSCT-alo systemic complications, being one of the main cGVHD, responsible also for increasing the levels of morbimortality[13]. The cGVHD is seen as a distinct syndrome that can affect virtually every major organ system, but most commonly involves skin, oral, vaginal and conjunctival mucosa, salivary and lacrimal glands and the liver[14]. As the oral cavity is a common region for presenting cGVHD, the recognition of these manifestations in initial stages is extremely relevant not only to improve the comfort, buccal health and function of the patient, but also to potentially allow long-term higher expectation of life[15].

The HSCT-alo can induce a reduction from 55% to 90% of the activity of both the major and minor salivary glands[16]. As consequence of these modifications in quality and quantity of saliva, immune changes, mechanical and chemical lesions occur leading to low resistance during dental demineralization, minor buffer capacity and increase of cariogenic microorganisms[17]. In the patient of this study, the involvement of salivary glands was identified through complaints reported and related to his deglutition and food intake. However, the salivary flow measured was 0.24 mL/min. Therefore, it is possible to affirm there was no irreversible damages, despite the characterization of severe hyposalivation. He was instructed to use oral lubricant to reduce taste-associated alterations, help to lubricate the oral cavity and the remineralization of carious lesions.

In this report, the patient had extensive carious lesions and there is narrative of the presence of caries in multiple dental elements associated to the salivary flow reduction resulting from cGVHD[18]. cGVHD associated caries is predominantly located in dental surfaces unlikely to be affected in healthy patients and similar to radiation-related caries[19]. The attempt to restore teeth with caries may fail and restorations can be less durable due to the absence of saliva in these patients[20]. In the present case, the treatment was conservative in the first moment, utilizing the cariostatic. Because of the reaction between its composition (silver fluoride diamine) and the mineral content of the tooth, obstruction of dentinal tubules and by the antienzyme action of the products of the reaction between silver fluoride diamine and the organic component, this product is a component able to prevent and arrest the carious activity, promote remineralization, increase the hardness of the carious dentin and can be used for dentin hypersensitiveness[21.] Despite not being a method utilized more frequently in pediatric patients, it was effective in the treatment of the referenced case, however, this method is limited to initial caries lesions and has low acceptance by the patients when indicated in previous teeth. Silver fluoride diamine acts to reestablish the dental integrity and consequently avoids that more invasive procedures as endodontic treatment happen to be needed[22]. In a second stage, restorations with composite resin were made to reestablish mastication, phonation and aesthetic of the patient. The treatment adopted, in addition of being satisfactory to control the carious lesions gave the patient back its self-esteem and trust as reported in the literature[23].

## CONCLUSION

In this clinical case, it is observed that silver fluoride diamine was effective in controlling the evolution of the caries and reducing odontalgia in the adult patient. It is evident the importance for dental surgeons to know the use of cariostatic in patients with changes in the quality and quantity of saliva, as patients with oral cGVHD, even in the absence of carious lesions with preventive finality, either pediatric or adult patients.

## CONTRIBUTIONS

Ana Carolina da Silva Souto and Daniel Cohen Goldemberg contributed for the wording and/or critical review with intellectual contribution. Gabriela de Assis Ramos and Andreia Cristina Melo contributed for the conception and/or design of the study; gathering, analysis and/or interpretation of the data. Héliton Spíndola Antunes contributed for the conception and/or design of the study; gathering, analysis and/or interpretation of the study data; wording and/or critical review with intellectual contribution. All the authors approved the final version to be published.

## DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

## FUNDING SOURCES

None.

## REFERENCES

1.
2. Lee SJ, Flowers MED. Recognizing and managing chronic graft-versus-host disease. Hematology Am Soc Hematol Educ Program. 2008:134-41. doi: https://doi.org/10.1182/asheducation-2008.1.134
3. Alencar FSL, Soares AC, Antunes HS. Tratamento das manifestações orais da doença enxerto contra hospedeiro crônica: revisão sistemática da literatura. Rev Bras Odontol [Internet]. 2016 [acesso 2019 nov 1];72(2):156-72. Available from: http://revodonto.bvsalud.org/scielo.php?script=sci_arttext&pid=S0034-72722016000200015
4. Meier JKH, Wolff D, Pavletic S, et al. Oral chronic graft-versus-host disease: report from the International Consensus Conference on clinical practice in cGVHD. Clin Oral Investig. 2011;15(2):127-39. doi: https://doi.org/10.1007/s00784-010-0450-6
5. Horwitz ME, Sullivan KM. Chronic graft-versus-host disease. Blood Rev. 2006;20(1):15-27. doi: https://doi.org/10.1016/j.blre.2005.01.007
6. Jagasia MH, Greinix HT, Arora M, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. the 2014 Diagnosis and Staging Working Group report. Biol Blood Marrow Transplant. 2015;21(3):389-401. doi: https://doi.org/10.1016/j.bbmt.2014.12.001
7. Young DA, Frostad-Thomas A, Gold J, et al. Secondary Sjögren syndrome: a case report using silver diamine fluoride and glass ionomer cement. J Am Dent Assoc. 2018;149(8):731-41. doi: https://doi.org/10.1016/j.adaj.2018.03.021
8. Carpenter PA, Kitko CL, Elad S, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: V. The 2014 Ancillary Therapy and Supportive Care Working Group Report. Biol Blood Marrow Transplant. 2015;21(7):1167-87. doi: https://doi.org/10.1016/j.bbmt.2015.03.024
9. Woo SB, Lee SJ, Schubert MM. Graft-vs.-host disease. Crit Rev Oral Biol Med. 1997;8(2):201-16. doi: https://doi.org/10.1177/10454411970080020701
10. Horst JA, Ellenikiotis H, Milgrom PL. UCSF protocol for caries arrest using silver diamine fluoride: rationale, indications and consent. J Calif Dent Assoc. 2016;44(1):16-28. Free PMC article. PMCID: PMC4778976
11. Gold J. Silver diamine fluoride arrests caries in primary teeth. J Evid Based Dent Pract. 2018;18(1):88-90. doi: https://doi.org/10.1016/j.jebdp.2017.12.007
12. Schwendicke F, Frencken JE, Bjørndal L, et al. Managing carious lesions: consensus recommendations on carious tissue removal. Adv Dent Res. 2016;28(2):58-67. doi: https://doi.org/10.1177/0022034516639271
13. Schubert MM, Correa MEP. Oral graft-versus-host disease. Dent Clin North Am. 2008;52(1):79-109. doi: https://doi.org/10.1016/j.cden.2007.10.004
14. Mays JW, Fassil H, Edwards DA, et al. Oral chronic graft-versus-host disease: current pathogenesis, therapy, and research. Oral Dis. 2013;19(4):327-46. doi: https://doi.org/10.1111/odi.12028
15. Imanguli MM, Alevizos I, Brown R, et al. Oral graft-versus-host disease. Oral Dis. 2008;14(5):396-412. doi: https://doi.org/10.1111/j.1601-0825.2008.01448.x
16. Santos-Silva AR, Feio PSQ, Vargas PA, et al. cGVHD-related caries and its shared features with other 'dry-mouth'-related caries. Braz Dent J. 2015;26(4):435-40. doi: https://doi.org/10.1590/0103-6440201300200
17. Nagler RM, Nagler A. The molecular basis of salivary gland involvement in graft--vs.--host disease. J Dent Res. 2004;83(2):98-103. doi: https://doi.org/10.1177/154405910408300203
18. Alborghetti MR, Corrêa MEP, Adam RL, et al. Late effects of chronic graft-vs.-host disease in minor salivary glands. J Oral Pathol Med. 2005;34(8):486-93. doi: https://doi.org/10.1111/j.1600-0714.2005.00347.x
19. Castellarin P, Stevenson K, Biasotto M, et al. Extensive dental caries in patients with oral chronic graft-versus-host disease. Biol Blood Marrow Transplant. 2012;18(10):1573-9. doi: https://doi.org/10.1016/j.bbmt.2012.04.009
20. Silva ARS, Alves FA, Antunes A, et al. Patterns of demineralization and dentin reactions in radiation-related caries. Caries Res. 2009;43(1):43-9. doi: https://doi.org/10.1159/000192799

21. Silva ARS, Alves FA, Berger SB, et al. Radiation-related caries and early restoration failure in head and neck cancer patients. A polarized light microscopy and scanning electron microscopy study. Support Care Cancer. 2010;18(1):83-7. doi: https://doi.org/10.1007/s00520-009-0633-3

22. Mei ML, Chu CH, Low KH, et al. Caries arresting effect of silver diamine fluoride on dentine carious lesion with S. mutans and L. acidophilus dual-species cariogenic biofilm. Med Oral Patol Oral Cir Bucal. 2013;18(6):824-31. doi: https://doi.org/10.4317/medoral.18831

23. Tan HP, Lo ECM, Dyson JE, et al. A randomized trial on root caries prevention in elders. J Dent Res. 2010;89(10):1086-90. doi: https://doi.org/10.1177/0022034510375825

24. Chu CH, Lo EC. Patients' satisfaction with dental services provided by a university in Hong Kong. Int Dent J. 1999;49(1):53-9. doi: https://doi.org/10.1111/j.1875-595x.1999.tb00508.x

**Recebido em 29/3/2020**
**Aprovado em 21/5/2020**